The Viscosity of the Blood.

By A. du Pré Denning, M.Sc. (Birm.), B.Sc. (Lond.), Ph.D. (Heid.), and John H. Watson, M.B., B.S. (Lond.), F.R.C.S. (Eng.).

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The full importance of a knowledge of the variations in the viscous resistance to be overcome by the blood in circulating through the capillaries and smaller vessels, and the actual significance of such data to the more thorough consideration of a large number of normal and pathological conditions, especially those of the circulatory system, has perhaps never been fully realised or appreciated either by physiologists or by clinicians in this country.

Although the subject of the viscosity of the blood has from time to time during the last 60 years attracted the attention of a few well-known investigators, yet, so far as we know, there has been no serious attempt to apply systematically the results of their researches to either the theory or practice of medicine.

The possibility of such investigations proving factors of consequence in certain physiological and pathological states has been strongly emphasised by Professor Osler in the 'American Journal of the Medical Sciences,' writing on the subject of chronic cyanosis with polycythæmia. "It is especially important to test the viscosity of the blood by accurate physical methods, and to determine the relation of the number of corpuscles to the viscosity."

But before entering into any details of the present series of experiments, it may be well to give here a simple interpretation of the term viscosity.

When a liquid is flowing steadily through a tube or pipe, the layers of the fluid immediately next to the walls of the containing channel are practically at rest, and consequently act as a drag upon the more rapidly moving layers nearer the central stream. Now the force exerted by the sum total of these "drags," or shears, that is, the viscous resistance offered to the fluid motion, is different for different liquids. Or we may say briefly that the *viscosity of a liquid is that property whereby it resists the relative motion of its constituent parts.*

Historical.

From experiments upon the flow of distilled water through capillary glass tubes placed horizontally, Poiseuille, in 1843, obtained data which find full expression in the well-known formula—

$$\eta = \frac{\pi(p-p')r^4}{8lQ},$$

where η = the viscosity coefficient,
$p-p'$ = the pressure gradient,
r = the radius of the capillary bore,
l = the length of the tube,
Q = the quantity of liquid flowing between two fixed marks in the time t.*

This law has been found to hold with great exactness not only for water, but for most homogeneous solutions. But when Poiseuille, and at a somewhat later date Regnault, examined the rate of flow of blood through a Poiseuille viscosimeter, they met with marked irregularities which they felt bound to ascribe to variations in the composition of the blood.

Except for Donders' reference to Poiseuille's results during the course of a discussion on hæmo-dynamics between Volkmann and Weber, these determinations of the blood viscosity were for many years practically ignored, probably owing to difficulties caused by coagulation. True, in 'Ludwig's Text-Book of Physiology,' published in 1861, we find references to the work of Poiseuille, Darcy, Dubuat, and Girard, and a statement to the effect that "die Geschwindigkeit veränderlich ist mit der Zusammensetzung der Flüssigkeit."

In this country, in 1874, Duncan and Gamgee made some experiments on the rate of flow of blood through tubes of narrow diameter, and observed that the rate of flow of blood taken directly from the vessels of a living animal is very much greater than that of defibrinated blood. This they explained by assuming that in the defibrinated blood there is a tendency for the blood corpuscles to run together and form small corpuscular masses or clumps, which would tend greatly to diminish the rate of flow of the liquid column in which they were suspended, and so might probably give rise to the observed deviations from Poiseuille's law.†

Ewald, working with defibrinated blood in 1877, found a value for its viscosity, which was about five times that of water.‡

A similar result was obtained in 1896 by Nicolls, who used a modified form of Poiseuille's viscosimeter;§ whilst Lewy, also working with defibrinated blood, gave its value as $3\frac{1}{2}$ times that of water.‖

* Poiseuille, 'Ann. d. Chim. et de Phys.,' 3 ser., vol. 1, p. 21, 1847.
† Duncan and Gamgee, 'Journ. Anat. and Physiol.,' vol. 5, p. 184, 1874.
‡ Ewald, 'Arch. f. Physiol.,' Leipzig, 1877.
§ Nicolls, 'Journ. Physiol.,' vol. 20, p. 407, 1896.
‖ Lewy, 'Arch. Physiol.,' vol. 70, Bonn, 1897.

In 1894, Graham Brown, writing in the Edinburgh Hospital Reports "On the Changes in the Circulation produced by a Rise in Temperature," pointed out the great diminution in the viscous resistance that occurs when defibrinated blood is made to pass through tubes heated to fever temperature, and applied his results to the explanation of certain phenomena of fever.

Brown also found that if defibrinated blood be rendered lake-coloured by alternately freezing and thawing, the rate of flow was increased, and that at varying temperatures the behaviour of the blood then approached tolerably close to that calculated by the Poiseuille formula.*

Hürthle, alone in 1896, and later with Russell Burton-Opitz, determined the values of the viscosity coefficient of the blood of different living animals by allowing it to flow directly from the carotid through a calibrated tube—simultaneous measurements of the outflow time and of the blood pressure being made. As a result of these experiments Hürthle states that (1) the coefficient of viscosity in any one species of animal is practically constant: that of a dog = 4·5 the value for water at 37° C.; that of a cat = 4·1, and of a rabbit = 3·2; and that (2) almost identically the same values were found for the viscosity of the blood of one and the same individual animal when tubes of various sizes and varying arterial pressures were employed—"from which we are to conclude that the suspension of the corpuscles in the blood does not seriously affect the application of Poiseuille's law to it as a fluid."†

R. Burton-Opitz, using Hürthle's instrument, found that intravenous injections of 0·7 per cent. saline caused an immediate and very distinct decrease in the viscosity, whereas equal amounts of distilled water apparently rendered the blood slightly more viscous. Further, the introduction of alcohol, either directly into the circulation or into the digestive tract, always rendered the blood more viscous: a much greater and more lasting increase appeared when the alcohol was injected into the stomach or duodenum.‡

Hirsch and Beck, employing a modified form of an Ostwald's viscosimeter connected to a constant-pressure apparatus, examined directly the blood of a number of persons: as a mean of their results, they suppose the normal value for the viscosity of human blood to be about five times that of water at 38° C., the lowest value they give being twice, and the highest nine times that of water. By means of this same instrument they examined the blood of 24 patients suffering from nephritis, but were unable to draw any definite conclusions.§

* Graham Brown, 'Royal Infirmary Reports,' Edin., 1894.

† Professor C. S. Sherrington, on Cardiac Physics, 'Allbutt's Medicine,' vol. 5, p. 476; Hürthle, 'Deutsch. Med. Wochenschr.,' August, 1897.

‡ Burton-Opitz, 'Pflüger's Archiv,' vol. 87, 1900.

§ Hirsch and Beck, 'Deutsch. Arch. für Klin. Med.,' vol. 69, p. 503, 1901, etc.

F. Lommel observed the influence of sweating upon the viscosity of the blood and found, as might have been expected, that in the great majority of cases the viscosity increases owing to the loss of water.*

A. Mayer, in 1901, calculated the coefficients of viscosity of serum, and of normal blood plasma in certain mammals, including man.†

G. Rossi, repeating and extending the observations of Burton-Opitz and A. Mayer, noted the influence of temperature of the viscosity of blood serum. He remarks upon a rather sudden change about the temperature of 45° C., and which is revealed by a marked diminution in the rate at which the viscosity declines and the electrical conductivity is at the same time increased.‡

Fano and Rossi, as a result of their investigations on liquid organic colloids, classify them in two groups according to their behaviour when certain substances as glucose, sodium chloride, etc., are added: in the one group, in which are placed such bodies as gum and starches, the viscosity is considerably diminished by these additions, whereas in the other group, in which are the albumens and various sera, but little effect is produced. However, after subjecting serum to dialysis they found on again adding the above substances that the mixture behaved like a solution of gum or starch; on the other hand, if the dialysed material were added to a solution of a gum, this conducted itself as the original serum.§

Again Fano and Rossi have confirmed Burton-Opitz's observation as to the influence of the thyroid on the blood. Experimenting on dogs and rabbits they found that the removal of the thyroids alone brought about some slight increase in the viscosity; but when the parathyroids also were removed, the viscosity rapidly increased to the time of death, which ensued sooner or later. They assume, therefore, that these bodies produce an internal secretion which is of the nature of an enzyme, whose function is to adjust the chemico-physical conditions of the blood, or, in other words, to regulate the viscosity.‖

C. Ferrai drew attention to the marked increase in the viscosity of the blood in asphyxia. He found that it may become double that of arterial blood, and increases in proportion to the increase of CO_2. One element in this increase may be the swelling of the corpuscles under the influence of CO, since the addition of CO_2 to serum, even to saturation, does not increase its viscosity.¶

* F. Lommel, 'Deutsch. Arch. für Klin. Med.,' vol. 80, p. 830.

† A. Mayer, 'Comp. Rend. de la Soc. de Biol.,' vol. 53, p. 1138, and vol. 54, p. 367, 1904.

‡ G. Rossi, 'Arch. di Fisiol.,' vol. 1, p. 500.

§ Fano and Rossi, 'Arch. di Fisiol.,' vol. 1, p. 609, 1904.

‖ Fano and Rossi, 'Arch. di Fisiol.,' vol. 2, 1905.

¶ C. Ferrai, 'Arch. di Fisiol.,' vol. 1, p. 305, 1904.

After we had commenced the experiments described in this paper, we learnt that Dr. R. J. Ewart, of Manchester, had been working at the same subject for some time. At our request he very kindly indicated to us the particular lines of investigation he had pursued. By a very ingenious though complex apparatus he found that the average value for the viscosity of defibrinated pig's blood with a capillary of 0·43 mm. radius is 3·8 times that of water, whereas that of dog's blood is 4·1, cat's, 4·2; whilst that of man is 3·14.

Further, he has carried out experiments on animals asphyxiated with excess of CO and CO_2, and found a rise in the viscosity. He also observed the result of substituting 0·6 per cent. saline for pig's serum, and confirmed the fact that an increase in the number of corpuscles in the blood resulted in an increase in the value of the viscosity coefficient.

Furthermore, he states that the viscosity coefficient of blood flowing through capillary tubes did not vary as the fourth power of the radius, as required by Poiseuille's law.*

Description of Apparatus.

The present experiments were undertaken in the first place to observe:—

(*a*) The influence of the number of corpuscles present upon the viscosity of the blood under varying conditions of temperature and pressure;

(*b*) The effect of the size of different capillary bores upon the rate of flow, again varying the number of corpuscles, temperature and pressure;

(*c*) The alterations, if any, caused by the addition of certain salts and other substances;

and, ultimately,

(*d*) To devise a viscosimeter for clinical purposes which would give reliable results with a very small quantity of blood.

A general idea of the actual arrangement of the various parts of the apparatus employed is most easily obtained from the photographic representation given in fig. 1 (A and B).

In order to study the effect of temperature, four thermostats were maintained at temperatures of approximately 32° C., 36° C., 40° C., and 44° C. respectively. Each thermostat consisted of a large glass beaker, of about 2 litres capacity, containing (*a*) a toluene-mercury gas regulator; (*b*) a thermometer; (*c*) a pear-shaped glass stirrer driven, in series with the other three stirrers, by a small electric motor, shown to the right of the photograph.

* Ewart, 'Thesis for D.Sc., Liverpool,' 1904.

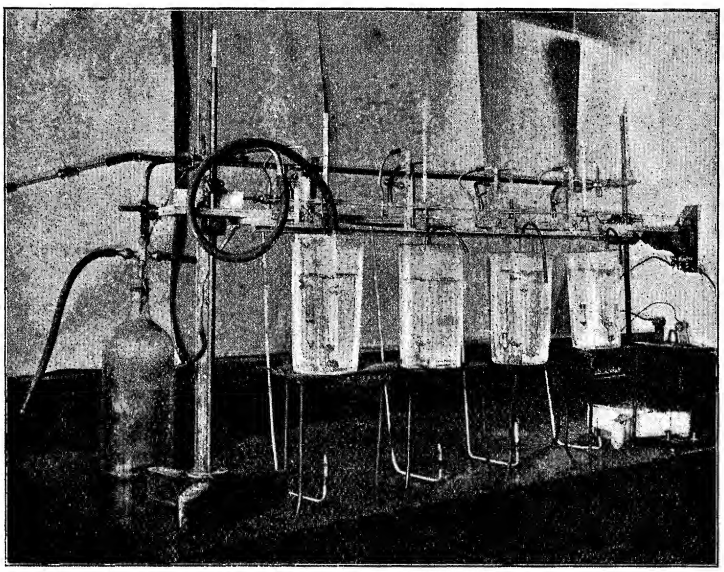

FIG. 1 A.

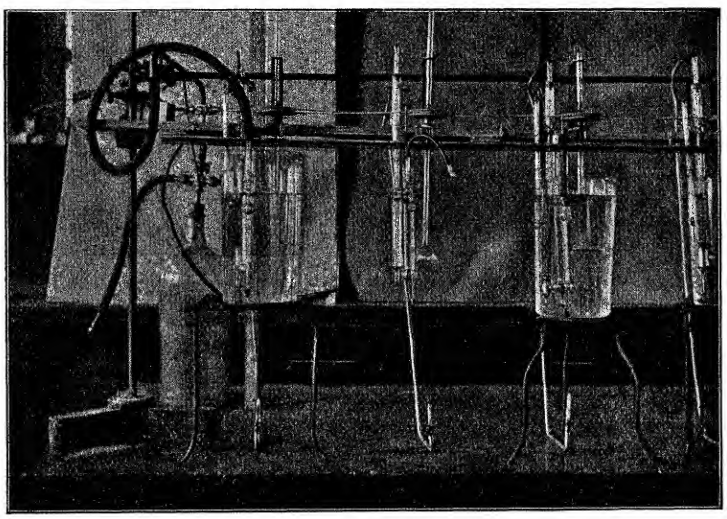

FIG. 1 B.

A diagrammatic representation of the contents of each thermostat, including the viscosimeters placed in position, is afforded by fig. 2. Two wooden bars shown are to be seen placed above the thermostats (fig. 1). To the posterior one were fixed the gas regulators, the thermometers and stirrers, whilst the front bar was notched, and into these notches were fitted the uprights of some special brass clamps, made to hold the viscosimeters vertically.

The kind of viscosimeter used was a slightly modified form of the

U-shaped instrument devised by Ostwald for the comparison of viscosities, and was, in our case, about 20 cm. in length.

A measured quantity of the blood, serum, or other fluid (about 2 c.c. with the smaller tubes) was introduced by means of a calibrated pipette down the wider arm into the larger bulb near the bend of the U. As will be seen from the diagram (fig. 3), the other limb of the viscosimeter was made of capillary tubing with a second and smaller bulb blown about 14 cm. above the bottom bend. The capillary tube above this smaller bulb was generally of wider bore and bent some four or five times away from the vertical, alternatively right and left as shown; in order to still further reduce as much as possible any irregularities or disturbances resulting from a too rapid sedimentation of the corpuscles at the bend joining the two limbs of the viscosimeter, the bend consisted of tubing of enlarged bore whilst the blood itself was well mixed by previously bubbling a slow stream of air through it before measuring the rate of flow.

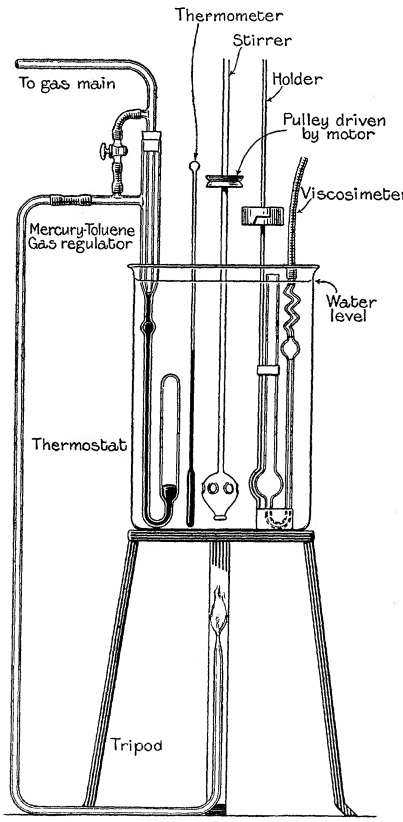

Fig. 2.—Diagram to show Arrangement of Apparatus in Thermostat.

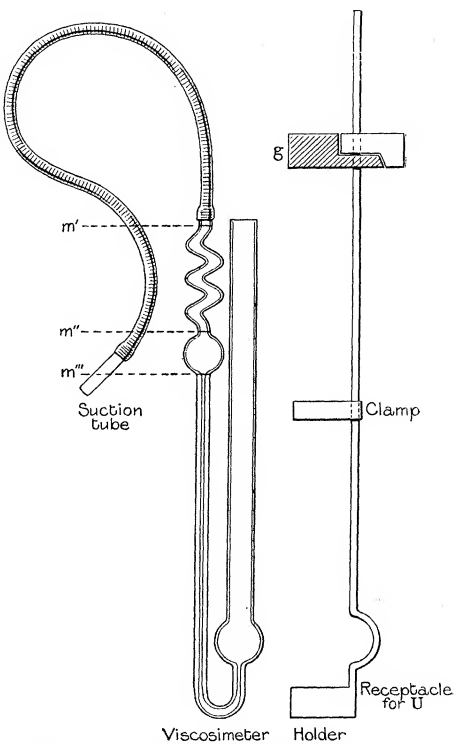

Fig. 3.—Diagram of Viscosimeter and Holder.

After sufficient time had been allowed to elapse for the viscosimeter and its contents to acquire the temperature of the bath in which it was placed, the blood or other fluid content was sucked up to the point marked (m') by means of a piece of rubber tubing affixed to the capillary arm, and then permitted to flow back through the bulb under the action of gravity. By means of a stop watch, reading to one-fifth of a second, the time taken for the end of the fluid column to flow from m'' to m''' was observed. By thus allowing the liquid column to get up a steady motion before observing its rate of flow we eliminate to a great extent errors resulting from differences of inertia of the various liquids examined.

If t' is the time in seconds for water at any particular temperature, σ' its specific gravity, whilst t is the time for the fluid examined and σ its specific gravity, then the relation between their viscosity coefficients η' and η respectively is

$$\eta : \eta' = \sigma t : \sigma' t', \quad \text{or} \quad \eta = \eta' \frac{\sigma t}{\sigma' t'}. \qquad \text{Formula (II)}$$

The absolute value taken for the viscosity coefficient of water, that is for η', at 35° was 0·007361 C.G.S. units, the value given by Thorpe and Rodger.

For those experiments in which the pressure gradient was varied the narrower limb of the viscosimeter was connected to a large Winchester bottle containing compressed air, by means of a long piece of pressure tubing wired on to the brass tube F.E. (*vide* fig. 4). Through the rubber bung in the neck of the Winchester was passed a +-shaped brass union which had taps on three of its arms; one of these, C, was in communication with a force pump, another, B, with a mercury manometer; and the third, A, was connected to the brass tube leading to the viscosimeter. A second brass tube, leading to an exhaust (filter) pump and provided with a tap at D, was soldered perpendicularly into F.E.

Before using this accessory apparatus the tap A was closed, air was forced into the Winchester until the manometer registered a convenient height, and the tap C then closed. The liquid in the viscosimeter was now drawn up to the topmost mark (m') by opening the tap D, and thereby connecting to the filter pump. When D was closed, A was opened, and the one observer with the stop-watch now noted the time of flow between the middle and lowest marks on the viscosimeter tube as before, whilst the other noted the initial and final pressure readings and manipulated the taps.

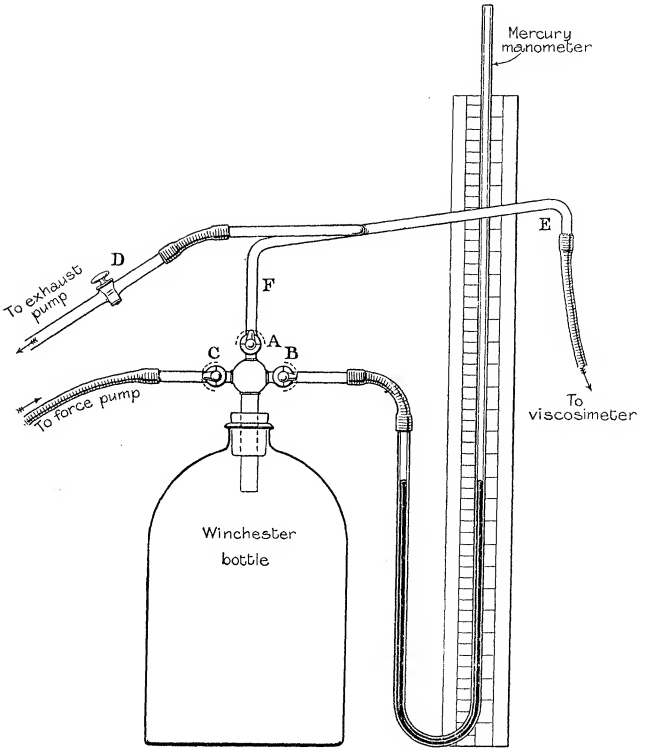

FIG. 4.—Accessory Pressure Apparatus.

Details of Experimental Results.

For the immediate purpose of these laboratory experiments, horses' blood was employed, since the corpuscular elements in such blood have been estimated by Sir John McFadyean to be practically identical in shape, though slightly less (in size) than those of human blood, viz., about 7 μ in diameter, and, moreover, horses' blood has this distinct advantage that, after an anti-coagulator has been added to it, the corpuscles and other cellular bodies are comparatively quick in settling, and soon leave a reasonably clear plasma. The objection may, perhaps, be raised that experiments carried out with animal blood are not, strictly speaking, applicable to human beings, but, as will be shown in the sequel, such results, although not numerically applicable, cannot but inevitably lead to deductions and conclusions, the principles of which are as fundamentally true for human physiology as for animal physiology.

Considering the heterogeneous structure of blood in general, and how variously the constituents of the blood of individual members of any one

species may differ among themselves, evidently if one desire to obtain strictly comparable results under varying conditions, say of the effect of corpuscles present, or of the effect of adding different quantities of the same or different salts, and to draw trustworthy deductions from the results of such experiments, it is absolutely essential that these experiments should, as far as possible, be carried out with blood obtained from the same animal or human specimen at one and the same time, and from the same part of the body, whilst the experimental conditions should be such as to allow the greatest amount of control of the particular influence it is desired to investigate. Clearly a vein or artery, probably in an unsymmetrical position with variable walls and connected directly to a complicated circulatory system with possible fluctuations of pressure, is not the ideal place to study in the first instance, say the effect of varying the number of corpuscles or that of different quantities of any particular salt.

The method we habitually adopted, after drawing up our scheme of experiments, was to place into a number of wide-mouthed stoppered jars just so much solution of a calculated strength of the anticoagulator chosen that, in general, when the stoppered jar was brought under the open vein of the animal and allowed to fill up to a definite mark, we knew that for every 95 c.c. of blood we had 5 c.c. of water and a known amount of the anticoagulator—or 5 c.c. of the anticoagulator when the same was not a water solution, *e.g.*, oil. (In the case of additions of $MgSO_4$, more water was present.) The jars thus filled were allowed to stand for two or three hours to settle. A large quantity of the supernatant plasma was then drawn off and centrifuged for two minutes.

To successive portions of this clear centrifuged plasma systematic additions of red cells were made, and a careful blood count taken from a well-shaken portion of this artificial blood by means of a Thoma-Zeiss hæmocytometer, just before the required amount was placed in the viscosimeters.

Of the fairly representative group of anticoagulators we tried—viz., potassium oxalate, sodium citrate, magnesium sulphate, peptone, leech extract, and olive oil—the two first proved to be the most satisfactory for our work. In Tables I and II will be found three series of observations made with different concentrations of each of these two anticoagulators at different temperatures and with varying numbers of red corpuscles suspended in similar plasma.

Under η in each sub-section are tabulated in absolute units the values found for the viscosity coefficient at the temperatures recorded in the first column on the left, with a blood containing the number of corpuscles per cubic millimetre stated at the head of the column. Under R is given the ratio

of this value of η for blood to that of water at 35° C. (viz., 0·007361 C.G.S. units).

The values given for the specific gravity are those used in making the necessary calculations of η by means of Formula II. Most of these values were obtained experimentally: from the data thus supplied the others have been obtained by interpolation on the assumption based on Hayem's statement that the specific gravity depends on the corpuscular richness of the blood, although it may be remembered that Schmaltz, judging from observations with his capillary pycnometer, concludes that the percentage of hæmoglobin, and not the number of corpuscles, is the main determining factor.

Table I.—Showing the Effect on the Viscosity Coefficient of varying (*a*) the number of red corpuscles, (*b*) the amount of salt added.

Viscosimeter bore = 0·6 mm. in diameter.

(A) Anticoagulator—5 c.c. of 0·1 per cent. potassium oxalate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$1 \cdot 6 \times 10^6$		$4 \cdot 0 \times 10^6$		$8 \cdot 4 \times 10^6$	
Specific gravity	1·030		1·034		1·042		1·055	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
31·8	0·0144	2·0	0·0200	2·7	0·0274	3·7	0·0637	8·7
35·0	0·0137	1·9	0·0186	2·5	0·0258	3·5	0·0554	7·5
40·0	0·0120	1·6	0·0165	2·3	0·0234	3·2	0·0456	6·2
44·8	0·0108	1·5	0·0153	2·1	0·0214	2·9	0·0376	5·1
Mean temp. coeff. ...	0·00028	—	0·00036	—	0·00046	—	0·00201	

(B) Anticoagulator—5 c.c. of 0·2 per cent. potassium oxalate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$1 \cdot 5 \times 10^6$		$4 \cdot 2 \times 10^6$		$6 \cdot 2 \times 10^6$	
Specific gravity	1·030		1·033		1·043		1·050	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
31·8	0·0137	1·9	0·0176	2·4	0·0254	3·5	0·0280	3·8
35·0	0·0128	1·7	0·0160	2·2	0·0231	3·2	0·0259	3·5
40·0	0·0118	1·6	0·0139	1·9	0·0205	2·8	0·0229	3·1
44·8	0·0106	1·4	0·0128	1·7	0·0182	2·5	0·0209	2·8
Mean temp. coeff. ...	0·00024	—	0·00037	—	0·00055	—	0·00055	

(C) Anticoagulator—5 c.c. of 0·3 per cent. potassium oxalate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$1 \cdot 4 \times 10^6$		$4 \cdot 2 \times 10^6$		$8 \cdot 4 \times 10^6$	
Specific gravity	1·030		1·033		1·043		1·055	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
31·8	0·0134	1·8	0·0167	2·3	0·0184	2·5	0·0287	3·9
35·0	0·0125	1·7	0·0157	2·1	0·0176	2·4	0·0272	3·7
40·0	0·0115	1·6	0·0140	1·9	0·0159	2·2	0·0257	3·5
44·8	0·0104	1·4	0·0126	1·7	0·0143	1·9	0·0236	3·1
Mean temp. coeff. ...	0·00024	—	0·00032	—	0·00032	—	0·00039	

Table II.

(A) Anticoagulator—5 c.c. of 0·5 per cent. sodium citrate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$2 \cdot 6 \times 10^6$		$4 \cdot 0 \times 10^6$		$8 \cdot 0 \times 10^6$	
Specific gravity	1·030		1·037		1·042		1·054	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
31·8	0·0140	1·9	0·0242	3·3	0·0296	4·0	0·0846	11·1
35·0	0·0128	1·7	0·0222	3·0	0·0268	3·7	0·0708	9.6
40·0	0·0114	1·6	0·0194	2·6	0·0233	3·2	0·0562	7·6
44·8	0·0103	1·4	0·0163	2·2	0·0198	2·7	0·0433	5·8
Mean temp. coeff. ...	0·00028	—	0·00061	—	0·00076	—	0·00317	

(B) Anticoagulator—5 c.c. of 1 per cent. sodium citrate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$2 \cdot 1 \times 10^6$		$4 \cdot 4 \times 10^6$ (?)		$5 \cdot 8 \times 10^6$	
Specific gravity	1·030		1·035		1·043		1·049	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
31·8	0·0142	1·9	0·0203	2·8	0·0264	3·6	0·0324	4·4
35·0	0·0132	1·8	0·0190	2·6	0·0244	3·3	0·0299	4·1
40·0	0·0118	1·6	0·0168	2·3	0·0221	3·0	0·0264	3·6
44·8	0·0106	1·4	0·0149	2·0	0·0196	2·7	0·0235	3·2
Mean temp. coeff. ...	0·00028	—	0·00042	—	0·00052	—	0·00062	

(C) Anticoagulator—5 c.c. of 2·5 per cent. sodium citrate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$2 \cdot 7 \times 10^6$		$5 \cdot 4 \times 10^6$		$9 \cdot 2 \times 10^6$	
Specific gravity	1·030		1·037		1·048		1·052	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
31·8	0·0138	1·9	0·0188	2·6	0·0253	3·5	0·0319	4·3
35·0	0·0128	1·7	0·0175	2·4	0·0234	3·2	0·0292	4·0
40·0	0·0115	1·6	0·0160	2·2	0·0207	2·8	0·0257	3·5
44·8	0·0109	1·5	0·0146	2·0	0·0185	2·5	0·0228	3·1
Mean temp. coeff. ...	0·00021	—	0·00032	—	0·00052	—	0·00072	

Table III.

(A) Anticoagulator—5 c.c. of 0·3 per cent. potassium oxalate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$3 \cdot 2 \times 10^6$		$6 \cdot 3 \times 10^6$		$12 \cdot 6 \times 10^6$	
Specific gravity	1·042		1·049		1·059		1·078	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
32·2	0·0139	1·9	0·0244	3·3	0·0356	4·9	0·1150	15·6
35·0	0·0131	1·8	0·0226	3·1	0·0340	4·6	0·1030	14·0
40·4	0·0122	1·7	0·0195	2·7	0·0309	4·2	0·0820	11·2
44·8	0·0111	1·5	0·0171	2·3	0·0285	3·9	0·0706	9·6
Mean temp. coeff. ...	0·00022	—	0·00058	—	0·00057	—	0·00352	

(B) Anticoagulator—5 c.c. of 0·1 per cent. potassium oxalate per 100 c.c.

No. of red corpuscles per cub. millim. ...	0		$2 \cdot 0 \times 10^6$		$4 \cdot 0 \times 10^6$		$8 \cdot 8 \times 10^6$	
Specific gravity	1·042		1·045		1·055		1·067	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
32·2	0·0141	1·9	0·0206	2·8	0·0330	4·5	0·0602	8·2
35·0	0·0134	1·8	0·0191	2·7	0·0313	4·3	0·0575	7·8
40·4	0·0120	1·6	0·0165	2·3	0·0282	3·8	0·0530	7·2
44·8	0·0110	1·5	0·0149	2·0	0·0264	3·6	0·0481	6·5
Mean temp. coeff. ...	0·00025	—	0·00045	—	0·00052	—	0·00096	

(C) Anticoagulator—5 c.c. of 0·5 per cent. sodium citrate per 100 c.c.

No. of red corpuscles per cub. millim. ... Specific gravity	0 1·042		$2·7 \times 10^6$ 1·047		$5·4 \times 10^6$ 1·055		$10·8 \times 10^6$ 1·072	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
° C.								
32·2	0·0143	1·9	0·0254	3·5	0·0375	5·1	0·1225	16·9
35·0	0·0135	1·8	0·0234	3·2	0·0350	4·8	0·1090	14·8
40·4	0·0123	1·7	0·0196	2·7	0·0306	4·2	0·0880	12·1
45·0	0·0111	1·5	0·0158	2·1	0·0268	3·7	0·0690	9·5
Mean temp. coeff. ...	0·00024	—	0·00075	—	0·00083	—	0·00417	

However, these specific gravity values are not of great importance, since the degree of accuracy obtainable with a Thoma-Zeiss or any form of hæmocytometer limits the degree of accuracy of the other measurements.

The Effect of Varying the Number of Corpuscles.—A most casual glance at either of these tables or at Table III will at once show that the increase of corpuscles always caused a marked increase in the values of η, and may under some circumstances result in a disproportionately large increase, the values in Table I ranging from about 1·5 times that of water at 35° C. to as much as 8·7 times (Sub-section A), or in Table III to 15·6 times the value for water (Sub-section A).

This result is, however, most simply brought out by the curves in fig. 5, in which are plotted a few values obtained at 35° C. (taken from Table I), with the number of corpuscles as ordinates and the value for η as abscissæ.

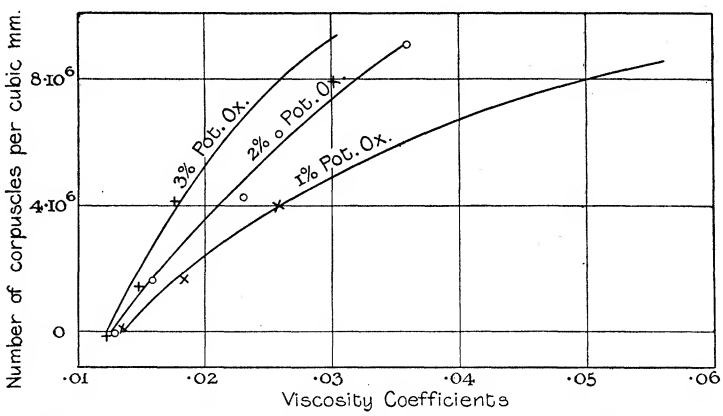

FIG. 5.—Curves showing Effect of Corpuscles on Viscosity with different amounts of Potassium Oxalate present. Temp. = 35° C. (*Cf.* Table I.)

Except for the different percentages of added anticoagulator, the blood was the same in each case.

Inasmuch as the curves are not straight lines, it is evident that the viscosity is not directly proportional to the increase of corpuscles, but rather that the former may increase very much more rapidly than the latter—obviously in the present case more so when 0·1 per cent. potassium oxalate was added than when it was 0·3 per cent. potassium oxalate. Similar curves, although not of the same curvature, were obtained when other experimental values were plotted. There are diverse reasons for the dissimilarity, as will be subsequently evident. In fig. 6, on precisely the same scale, are

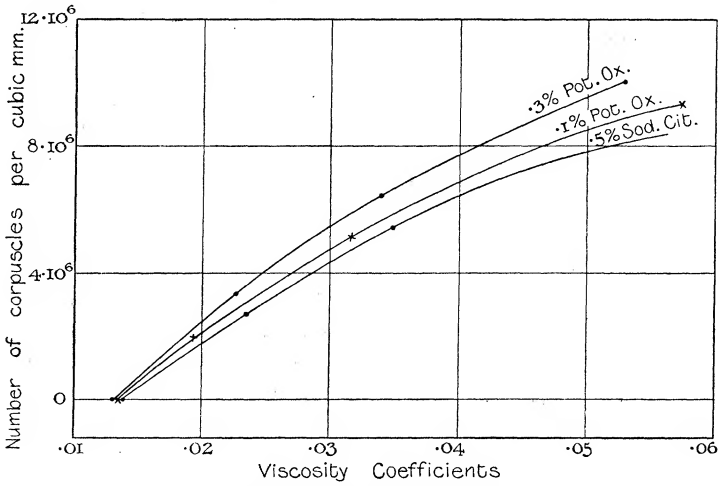

Fig. 6.—Curves plotted from Table III. Temp. = 35°.

recorded results obtained with a different blood, namely, that of a young horse (3 years old), whilst the former was that of an old one (about 18 years old). But, though the same strengths of anticoagulators were again added, it is apparent that the increase in viscosity was here much greater for any given increase in the number of corpuscles. Indeed, from the trend of these three curves it may well be supposed that a blood containing upwards of 20×10^6 corpuscles per cubic millimetre would have taken longer to flow through the particular viscosimeter tubes used than the same quantity of treacle would have done. It may further be observed that the differences of the influence exerted by each of the three anticoagulators are not so strongly marked in this set of curves.

Such results as the foregoing are obviously in direct contradiction to Hürthle's view which Professor Sherrington quotes in Allbutt's 'Medicine,' and to which reference has already been made, viz., that "the suspension of

the corpuscles in the blood does not seriously affect the application of Poiseuille's law to it as a fluid."

From the results of some of his experiments, Dr. Ewart has arrived at the rather astonishing result that a blood containing $5{\cdot}10^6$ corpuscles per cubic millimetre requires least expenditure of energy on the part of the heart to drive a definite quantity of it in unit time past any particular cross-section, or, as he says, human blood containing five million corpuscles per cubic millimetre is mechanically the most efficient and economical. Similar calculations from our observations, however, have not afforded the slightest confirmation of such an unexpected result. Nor do Dr. Ewart's own results always agree with it.

It would, moreover, appear to us that the deduction is by no means justifiable or, indeed, valid, inasmuch as the calculations rest upon direct comparison between three different kinds of blood, viz., pig's blood for the value with the $6{\cdot}10^6$ corpuscles, human blood for that with $5{\cdot}10^6$, and a mixture of human and pig's serum for the lower values. As will be seen later, the mere number of corpuscles present is far from being the only factor which may influence the viscosity of a blood.

The Effect of Change of Temperature.—At the bottom of each sub-section is given the change in viscosity which resulted from a change of temperature of 1° C., that is, the mean temperature coefficient at temperatures of about blood heat. And if we take any one series, it is apparent that this temperature coefficient increased with increase in the number of corpuscles. In figs. 7 and 8 are plotted the values of the viscosity coefficient found at different temperatures for the three series, Table II (B), and Table III (A)

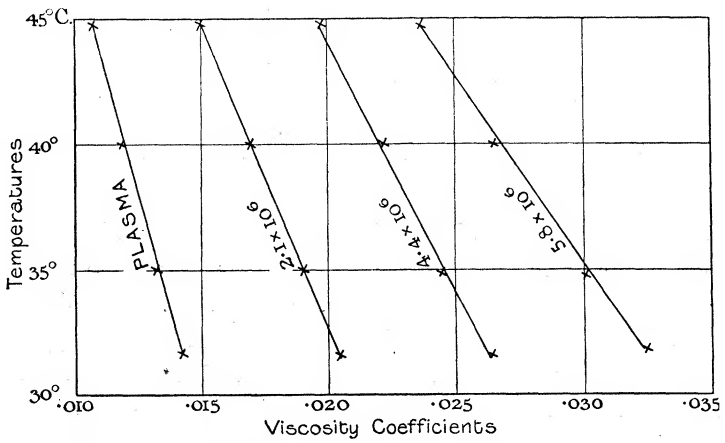

FIG. 7.—Curves showing Temperature Effect with varying number of Corpuscles. (*Cf.* Table II [B].)

and (C) respectively—the number of corpuscles being given by the side of each curve. The differences in slope obviously form a graphical confirmation of the foregoing remarks with regard to the temperature coefficient, whilst the numerical details supplied in the tables show that it ranged from about 0·0002 to 0·004. Although the temperature gradients are represented by straight lines in these diagrams, experiments over a larger range showed that the change of viscosity with temperature was by no means a linear function.

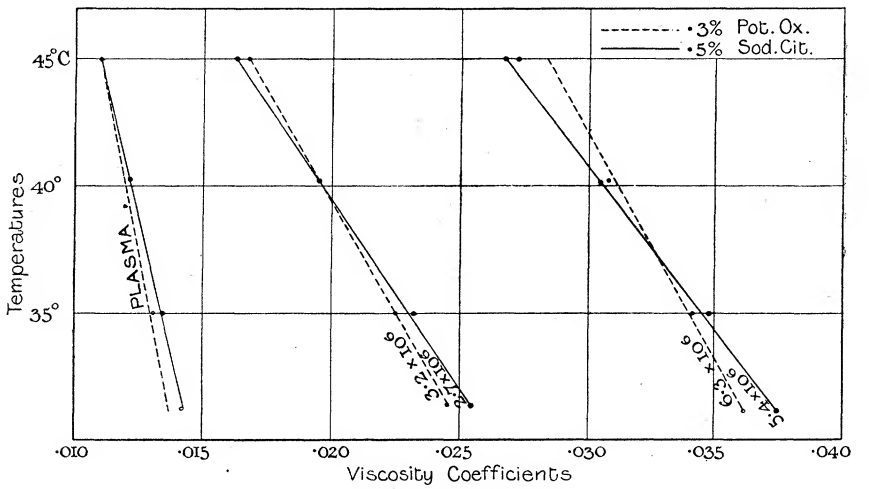

FIG. 8.—Curves contrasting Temperature Variations after Additions of Potassium Oxalate and Sodium Citrate solutions respectively. (*Cf.* Table III [A] and [C].)

The Effect of Added Salts, etc.—The possible influence which the addition of salts may have upon the relation of the viscosity to the number of corpuscles will have already been gathered both from the tables of numerical results and from the curves, of which mention has so far been made. From fig. 5 it will appear that the addition of 0·3 per cent. potassium oxalate reduced the viscosity coefficient of blood containing $8{\cdot}4 \times 10^6$ corpuscles per cubic millimetre to less than half of that with blood containing 0·1 per cent. potassium oxalate, but otherwise similar in composition; whereas from fig. 6 the difference caused by the added salts is hardly noticeable with the three anti-coagulators mentioned in the figure. Again, fig. 8 would apparently indicate that 0·3 per cent. potassium oxalate could evidently reduce the viscosity more than 0·5 per cent. sodium citrate, whilst the mean temperature coefficient would seem to be larger for the sodium citrate solution, inasmuch as the potassium oxalate temperature curves are steeper.

Although it is evident in the cases just considered that the addition of

these salts decreased the viscosity, yet the extent of the reduction is apparently quite a variable quantity; indeed it depends to a large extent upon the internal composition of the particular blood examined, and on the initial action of its constituents and the added salts.

Ewart has also observed that additions of dilute saline lowered the viscosity, whereas an increase of acidity or alkalinity, as well as the addition of many neutral salts, caused an increase in viscosity. The fall in viscosity he attributes to a reduction of the quantity of albumin, etc., and the fall of proteid strength.

When considering the effects of changing the concentrations of the salt solutions, etc., present, it should be borne in mind that whenever an animal cell is brought into a strong salt solution, the osmotic pressure of which is greater than that of the cell sap, the cell contracts and becomes flaccid, owing to the passage outwards of certain constituents of the sap, whilst the effect of placing the cell into a dilute solution, the osmotic pressure of which is less than that of the cell sap, will cause the cell to expand and even eventually burst. As hæmatocrite and other experiments have shown, the blood corpuscles are affected in the same way; in strong solutions they are crenated; in dilute solutions they may burst and allow the red colouring matter to pass into the surrounding liquid. Duncan and Gamgee have shown that laking causes a diminution of viscosity.

But the study of the effect of changing the concentration of the chemical bodies present in the blood is still further complicated by the fact that the protoplasmic cell walls may vary considerably in their permeability. For instance, Dr. Loeb, of Chicago, asserts that the eggs of sea urchins, if placed in concentrated solutions of NaCl, die at once, but show increased vitality if a tiny quantity of certain metallic salts be present. Experimenters with colloidal liquids have frequently noticed how the addition of certain reagents may sometimes bring about changes in some particular property of the colloid, which are altogether out of proportion to the weight or bulk of the added reagent, *e.g.*, one drop of a weak $FeCl_3$ solution to about 50 c.c. of colloidal Fe $(OH)_3$ has been observed to lower the viscosity of the latter by 500 per cent.* Whilst Majorana† and Schmaus‡ have found that the smallest traces of the chloride were sufficient to destroy all traces of the magnetic double refraction of the colloidal iron hydrates, etc.

The study of the influence of various salts upon the viscosity of the blood is obviously a province in which much work has yet to be done in order to

* *Vide* Denning, 'Ueber die Viscosität, etc., des colloidalen Eisenoxydhydrates, Inaugural-Dissertation, Heidelberg, 1904.

† Qu. Majorana, 'Rendic. Acc. del Lincei,' II, vol. 1, p. 374, etc., 1902.

‡ Schmaus, 'Ann. der Physik,' vol. 10, p. 658, vol. 12, p. 186, 1903.

find out which chemical bodies most strongly affect the viscosity of the blood under certain conditions, since this is clearly of importance in considering changes in the circulatory system. Mention may be made of the recent researches of G. Stodel on the biological importance of small quantities of colloidal bodies in the treatment of certain infective diseases, etc. An investigation of the effects of these bodies on the viscosity of the blood may conceivably prove most profitable.

A subsequent series of determinations some six days later gave practically the same results.

The Viscosity Coefficients for Various Plasmata and Sera obtained from the blood of the same animal are placed together in Table IV, with the anti-coagulator into which the blood was received at the head of each column.

Table IV.—Showing Values of the Viscosity Coefficients found for various Plasmata and Sera.

Anticoagulator.	Salted plasmata.		Sera.		
	0·3 per cent. potassium oxalate.	12·5 per cent. $MgSO_4$.	Peptone.	Leech extract.	Olive oil.
° C.					
31·8	0·0139	0·0141	0·0136	0·0126	0·0125
35·0	0·0131	0·0134	0·0128	0·0119	0·0119
40·0	0·0122	0·0124	0·0116	0·0104	0·0105
44·5	0·0110	0·0115	0·0105	0·0098	0·0099

With horses' blood, as is well known, there follows a rapid subsidence of the corpuscles: consequently it was easy to siphon off small quantities of the supernatant liquid from each specimen. In the case of the first two specimens (namely, with potassium oxalate and $MgSO_4$) observations were taken before coagulation had occurred, *i.e.*, we were dealing with plasma; whilst in the case of the last three clotting had occurred before estimations were attempted. Having found such small variations in the viscosity values for the plasma and serum with the conditions under which these experiments were made, we did not pursue this question further, inasmuch as our chief object was to investigate those factors which play a predominant part in determining the viscosity of the blood.

The Effect of Varying the Capillary Bore.—When it is remembered that blood is really a very complex colloidal suspension or emulsion, containing numerous particles, corpuscles, and other cellular elements, in a feebly viscous matrix, we may well imagine that the rate of increase of the viscosity coefficient with each fresh addition of corpuscles, etc., will depend largely on

the size of the capillary bore of the viscosimeter, and with different bloods on the relative sizes of the corpuscular elements. Naturally we cannot expect the addition of the corpuscles *per se* as semi-solids, and their variations in size, to have any appreciable effect on the viscosity unless they are to pass through capillary tubes of radius comparable with their own dimensions. Against Hürthle's statement, already mentioned, that "almost identically the same values were found for the viscosity of the blood of one and the same individual animal when tubes of various sizes and varying arterial pressures were employed," it is to be urged that his method of attacking the question did not admit of his obtaining a sufficient experimental range from which reliable conclusions could be drawn. From the experimental results recorded in Table V, for which a large quantity of blood was available, whilst viscosimeter tubes of bores varying from 2 mm. to 0·3 mm. could be directly employed, and "artificial" blood mixtures with widely differing numbers of corpuscles easily made up, it will be seen that the smaller influences of each successive alterations become, as it were, of magnified importance, when viewed as parts of a bigger scheme, and show at once that blood containing a large number of corpuscles encounters considerably greater resistance to its flow than is to be expected from an application of Poiseuille's law, in its

Table V.—Showing the Variation of the Viscosity Values with the size of the Capillary Bore.

Capillary bore.	2 mm.		1 mm.		1·6 mm.		0·3 mm.	
Temperature.	η.	R.	η.	R.	η.	R.	η.	R.
	Plasma from 1 per cent. potassium oxalate.							
32°·2	0·0130	1·8	0·0139	1·9	0·0140	1·9	0·0141	1·9
40·4	0·0110	1·5	0·0119	1·6	0·0121	1·6	0·0121	1·6
	Plasma + 3·6 × 10^6 corpuscles per cubic millimetre.							
32·2	0·0202	2·7	0·0241	3·3	0·0272	3·7	0·0338	4·6
40·4	0·0180	2·4	0·0221	3·0	0·0244	3·3	0·0304	4·1
	Plasma + 6·0 × 10^6 corpuscles per cubic millimetre.							
32·0	0·0265	3·6	0·0333	4·5	0·0402	5·5	0·0546	7·4
40·4	—	—	0·0302	4·1	0·0368	5·0		
	Plasma + 9·6 × 10^6 corpuscles per cubic millimetre.							
32·0	0·0474	6·5	0·0562	7·5	—	—	0·0982	13·4
40·4	0·0428	5·8	0·0513	7·0				

passage through fine capillaries than it does through tubes of comparatively wide bore.

During the consideration of the series of observations contained in Table III we drew attention to the diversity of the results that might be obtained with the blood of different animals, even though it contain exactly the same number of corpuscles and the same amount of added salt or anticoagulator. This at first sight may seem very contradictory; but remembering how the red cells vary in size not only in different species but in the individuals of the same species, we would suggest, from considerations of physical and natural phenomena, that this dissimilarity may be due to quite small variations in the dimensions of the red cells and the amount of the attendant colloidal matter (*e.g.*, proteids, etc.) enveloping them as central nuclei in much the same way as, for example, the solid and semi-solid particles in brackish water are coated with slime, or as the planets surrounded by their attendant atmospheres, or perhaps more nearly resembling the richly colloidal *Schaummassen* and *Schaumflocken* in Professor Quincke's theory of colloidal solution.*

And, indeed, here it might well be remarked that just as all purely colloidal solutions which have been standing for any length of time tend to become more viscous by reason of the growth of existing colloidal nuclei and the formation of new ones at the expense of the colloidal materials in the sustaining fluid medium, so we may similarly expect that a badly circulating but otherwise healthy blood with the average amount of colloids would, as a result of its partial stagnation, likewise tend to become more viscous, and so, by thus still further decreasing the circulation through the whole system, and more especially in the peripheral vessels, eventually give rise to some form of cyanosis, unless counteracted in other ways.

As showing the comparative unimportance of such changes to the rate of flow through the veins and other large vessels, we give, in Table VI, a few comparative values obtained with a tube of 3·5 mm. and a capillary of 0·6 mm. It has, of course, long been recognised that Poiseuille's law only holds for homogeneous solutions in narrow tubes if the rate of flow be slow, which certainly was not the case with the larger tube in question, as may, perhaps, be inferred from the low value found for the plasma. But for our purpose this is immaterial, since the result clearly illustrates the fact that changes in the viscosity are only of importance in the circulation of the blood through the finer channels of the circulatory system. For example, it will be seen that, with a blood containing some 16 million red corpuscles per cubic millimetre, the value for η was only 5·3 times that for water at

* *Cf.*, *e.g.*, G. Quincke, 'Ann. d. Phys.,' vol. 9, pp. 969—1045, 1902.

Table VI.—Giving Comparative Values between a Wide Tube and a Capillary.

Bore.	3·5 mm.				0·6 mm.	
Temperature.	Plasma.		Plasma + $16{\cdot}10^6$ corpuscles per cub. millim.			
	η.	R.	η.	R.	η.	R.
° C.						
32·2	0·0091	1·24	0·0386	5·3	0·208	28·4
45·0	0·0086	1·17	0·0288	3·9		
18·2	—	—	0·0745	10·2	0·541	74·0

35° C. with the big tube, but 28·4 with the smaller, whilst determinations made at the atmospheric temperature, viz., 18°·2 C., gave values of 10·2 and 74 respectively, showing the absolute futility of taking measurements of viscous blood without simultaneously recording the temperature and the approximate bore of the narrow portion of the viscosimeter, for example, as Dr. F. Parkes Weber* has neglected to do.

The Effect of Change of Pressure.—The results of a series of experiments carried out with the accessory apparatus, shown in fig. 4, are given in Table VII. The pressure range adopted lay between 17·6 cm. Hg and 2·2 cm., or was somewhat larger than that generally met with in the human system. The corrected values for the pressures, that is to say, the readings of the manometer and a correction for the difference of level of the blood in the viscosimeter tubes, are tabulated in the first column of each sub-section, the outflow time in seconds in the second column, and the calculated values of η in absolute units in the third. Obviously if the different specimens of blood obeyed Poiseuille's law for these changes of pressure the product "pressure × time" should be a constant, that is, the calculated values for η should be constant. For the result recorded in the first two sub-sections this will be seen to hold within the limits of experimental error.

But for the blood containing $6{\cdot}10^6$ corpuscles per cubic millimetre, and more especially for that $9{\cdot}6 \times 10^6$ in a tube of 3 mm. diameter, it is evident that a gradual decrease of pressure resulted in a gradual increase in the η. Or with a fine capillary (*e.g.*, animal capillaries) the time of outflow is not simply inversely proportional to the pressure as required by the Poiseuille formula. With tubes of wider bore, and over the same range of pressure and number of corpuscles, such marked deviations were not detectable.

* 'Clinical Society's Transactions,' 1904.

Table VII.—Showing Values of η under Different Pressures with varying Number of Corpuscles.

Capillary bore = 0·3 mm. Temperature = 32°·2 C.

Pressure (corr.).	Time of outflow.	η.	Pressure (corr.).	Time of outflow.	η.
Plasma.			+ 3·6 × 10^6 corpuscles per cubic millimetre.		
Cm. Hg.	Secs.	C.G.S. units.	Cm. Hg.	Secs.	C.G.S. units.
15·6	22·8	0·0138	12·8	65·8	0·0332
13·5	27·4	0·0143	10·1	85·0	0·0338
11·3	33·4	0·0145	7·7	112	0·0342
8·0	47·2	0·0145	5·0	168	0·0332
4·6	80·3	0·0142	2·2	410	0·0347
2·6	141·7	0·0139			
+ 6 × 10^6 corpuscles per cubic millimetre.			+ 9·6 × 10^6 corpuscles per cubic millimetre.		
16·0	85·0	0·0538	17·6	138·0	0·0964
14·4	95·2	0·0550	15·6	158·0	0·0972
10·4	134·0	0·0552	10·8	229·4	0·0984
7·3	188·0	0·0545	8·2	306·0	0·0998
—	—	—	5·6	306·0	0·1079

With very fine tubes and long times of outflow it may be mentioned that the segregation of corpuscles at the bottom of the viscosimeter is liable to cause annoying irregularities, involving frequent repetition after the blood has been well mixed by gently bubbling a slow stream of air through it. From the curves of fig. 9 which, it will be noticed, are practically rectangular

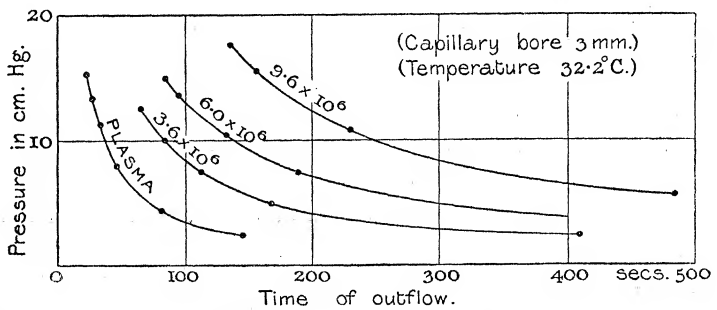

Fig. 9.—Curves showing the Relation between Outflow Times and Pressures with varying amounts of Corpuscles.

hyperbolas of decreasing curvature, some interesting inferences may be drawn. The outflow times of fig. 9 have been plotted as abscissæ and the

pressures as ordinates. Over the present range of pressures it will be seen that a small change of pressure at, *e.g.*, 10 cm. Hg, will cause a greater diminution of the outflow time for blood poor in corpuscles than for blood rich in corpuscles and, as a consequence of this, in the human circulatory system we should find such changes producing a much more rapid return of the arterial blood to the heart. Further reference will be made to this point, however, in the subsequent discussion of the bearing of this and foregoing results on the disorders of the circulatory system. Below about 5 cm. pressure the curves would seem to indicate that this effect is not so much *en evidence*. Similar results and curves, though naturally with smaller values for η, were obtained when these observations were repeated at higher temperatures.

Summary.

The chief results of the foregoing investigations may be briefly summarised in the following general statements:—

1. The decrease in viscosity for each degree rise of temperature is less marked for plasma than for blood.
2. It is also decidedly less for blood containing few corpuscles per cubic millimetre than for blood containing many corpuscles per cubic millimetre.
3. For any given temperature and capillary bore an increase in the number of corpuscles causes an increase in the viscosity (*cf.* Tables I–III), though it is to be remarked that—
   (*a*) with tubes of wide bore a very large increase in the number of corpuscles is necessary to cause an appreciable effect (*cf.* Table VI), whereas
   (*b*) with small capillaries a slight increase in the number of corpuscles always causes a very marked increase in the viscosity (*cf.* Table V).
4. With a given number of corpuscles the rate of flow through any particular tube down to about 3 mm. in diameter is, over the range of pressure occurring in living organisms, practically directly proportional to the pressure.
5. A given increase of pressure exerts a much greater accelerating effect on the rate of flow through tubes of fine calibre than through tubes of wider bore.
6. The influence of a definite increase of pressure on the time of flow is slightly less for blood at fever temperatures than for the same blood at lower temperatures.
7. The pressure influence is also greater for blood containing a large

number of corpuscles than for blood containing few (*cf.* curves in Curve-Table 9).

8. The addition of certain chemical reagents decreases the viscosity, whilst other substances may increase it.

An Indication of the Bearing of Viscosity upon the Circulation of the Blood.

In the next few pages we wish very briefly to indicate the import of such results as the foregoing in any consideration of the mechanism of the circulation of the blood. For this purpose we may with advantage regard the human circulatory system from a simple mechanical point of view, as a well-arranged though very complex net-like labyrinth of elastic pipes, namely, the arteries and veins, connected with a central pumping-station, the heart, which maintains a constant circulation of a viscous fluid, having a peculiar and variable consistency—the blood; and to this simplified circulation endeavour to apply the above conclusions, when alterations occur affecting the whole or any one part of this system; for it is evident at once that any disturbance in the mechanism may arise from—

1. Conditions that interfere with the normal activity of the heart;
2. From alterations in the calibre of the blood vessels;
3. From changes in the amount or the composition of the blood with the consequent variations in viscosity.

Effect of Temperature.—For instance, it is well known that in ordinary healthy persons, as a result of vigorous exercise, the temperature may rise to 101° F., or even higher, and there is associated with this condition of hyperthermia an increased frequency of the heart beat, and at the same time dilatation of the peripheral blood vessels. The result of these changes is to increase the velocity of the blood flow: firstly, because the increased temperature will give rise in itself to a diminution in viscosity; and secondly, the increased calibre of the vessels reduces the peripheral resistance. As a nett result, there is a more rapid filling of the heart, but for each individual beat there is less resistance to be overcome, and consequently the heart is saved an appreciable strain; that is to say, we have a simple illustration of nature's way of mechanically adjusting the balance of the circulatory system so as to compensate for the extra work thrown upon the heart.

Passing from this normal physiological reaction we are led to consider the conditions met with in fever. In the early stages, with a raised temperature and a rapidly beating heart, there is an undoubted increase in the peripheral resistance (Maragliano)* and, moreover, the composition of the blood is altered—there being invariably a slight leucocytosis and an addition to the

* Maragliano, 'Zeit. f. Kl. Med.,' vol. 14, p. 309, 1888.

metabolic products contained in the circulating blood, which alterations in themselves tend to raise the viscosity.

Apart, therefore, from the raised temperature, these changes in the mechanism would tend to throw more work upon the heart, which, however, owing to its great reserve force, can respond for a time; fortunately in most cases, before it begins to flag, the second stage, or fastigium, is reached, in which the peripheral resistance is relaxed. This loss of vasomotor tone is always a noticeable feature at this period, and as a result the work of the heart is once more considerably lightened. Experimental evidence has given abundant proof of the marked incr ase in the rate of flow that follows upon a widening of the conducting char ıel; and further, our results have shown that with fine capillaries this influence is considerably greater than the fourth power of the radius, as is stated in Poiseuille's formula.

We would emphasise here again the marked influence of temperature on the viscosity of all fluids; for instance, the viscosity of water at 30° C. is one-half of what it is at 0° C., whilst with blood containing some $5{\cdot}10^6$ red corpuscles per cubic millimetre, our Tables, in some cases, show as large a change as 3 per cent. per 1° C.

Now the usual reasons given for the more rapid beating of the heart are: (1) the disturbance of the nerve centres; (2) the direct action of the patient's overheated blood upon the heart muscle. This last statement is founded upon the experimental ground that by perfusing an isolated mammalian heart with warm blood there results a more frequent contraction. Now we would add a third reason: *the more rapid filling of the heart* as a result of (1) the lessened resistance; (2) the diminished viscosity; therefore, as a consequence of the increased rate of flow, the diastolic period of the heart is lessened, and the ventricles refill much more quickly.

To quote Dr. Graham Brown, "a febrile temperature may be considered as a boon to the organism, in that it will allow the blood to circulate faster or it will save the work of the heart"; a deduction of the utmost importance, and one which, so far, has apparently received very little notice.

Effect of Change in Calibre of Vessels.

Again, alterations in the capacity and in the actual structure of the vessels are far from uncommon as the results of disease. The lesion which may follow an infection or intoxication is, unfortunately, not limited, but usually involves, step by step, the whole arterial tree. We may take as an instance of this condition the arterio-sclerosis which occurs in chronic nephritis; in these cases it is the smaller vessels that are attacked first and their lumen

gradually encroached upon. We know that the rate of flow in capillaries is much slower than in the arteries and veins, for it is here that the greatest resistance is met with, and consequently most of the driving pressure is spent; if, therefore, the arteries leading to the capillary area are contracted in the slightest degree the sum total of the increased resistance in such an extensive change as occurs in Bright's disease must make a very marked difference in the work necessary to bring about a minimum circulation through the capillaries, that is to cause a blood velocity of the order of 0·5 mm. per second. We have already seen that the frictional resistance produced by alteration in the smaller capillary bores increases very rapidly with diminution in size, more especially with the finer periphery vessels. In order, therefore, that the mechanism be fully compensated for the narrowing of the smaller channels, there must be either: (1) an increase in the driving force, that is, a more powerful heart beat, or (2) a diminution in the viscosity of the blood itself. As is well known, the compensation in Bright's disease is usually brought about by an hypertrophy of the heart itself; and apart from any changes which may occur in the constitution of the blood (which indeed often shows an increased viscosity) we consider that the enormous increase in peripheral resistance occasioned by the general contraction of the smaller vessels affords an ample explanation of the vexed question of the cause of cardiac hypertrophy which is so truly necessary to bring about an adequate circulation. Furthermore, we do not see any reason to reinstate Bright's theory that there is some unknown substance circulating in the blood which acts directly on the heart muscle, as Hirsch and Beck have recently attempted.

Effect of Changes in the Composition of the Blood.—With regard to the changes in the composition and constitution of the blood, which will give rise to variations in the viscosity and, as a consequence, affect the circulatory mechanism, one can only remark here upon their infinite variety. Taking the plasma alone there may be (1) an increase or diminution in its volume; (2) proteid strength may be altered; (3) salts may be deficient or in excess; (4) metabolic products, *e.g.*, alloxuric bases and other nitrogenous derivatives abnormally abundant; (5) excessive saturation with gas, for instance CO_2; (6) presence of ferments, organised and unorganised. All these in themselves are capable of altering the viscosity values.

Or again, if we consider the corpuscles, viscosity changes can be produced by (1) variations in number of reds; (2) variations in number of whites; (3) variations in size.

We may here make mention of the following interesting experiments of Ferrai on the viscosity of the blood in partly asphyxiated animals. In his

investigation with serum alone he found that the addition of CO_2, even to saturation, produced little or no change, whilst in the case of blood there was a noticeable increase in each addition of CO_2. This he attributed in part to the swelling of the corpuscles; his surmise was proved to be correct by measuring the volume of the corpuscles by means of the hæmatocrite (it was found to be increased).

Before we could make any investigation on the viscosity of the human blood it was necessary to devise an instrument capable of giving results with a small quantity of blood, since the instruments in use on the Continent required more blood than was obtainable or even permissible in this country from patients. Hirsch and Beck had been experimenting with 2 cm. of blood, whilst Dr. Parkes Weber's instrument requires even larger quantities of blood. Dr. Ewart had devised an instrument, but it was too complicated and required too many accessories for ward work.

Fig. 10 shows the form of instrument which we ultimately adopted and which is fully described in Appendix I.*

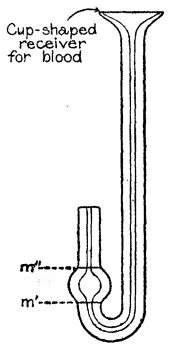

FIG. 10.—Clinical Viscosimeter for use with small quantities of Blood.

With this viscosimeter numerous observations have been made upon healthy individuals with fairly constant results, the average value found being roughly about five times that of water.

The following Table (VIII) contains viscosity values for the blood of five men in the best of health, with a record of their temperature and blood count.

Table VIII.—Viscosity Values in five Healthy People.

—	Temperature.	Blood count reds.	Time compared with water.
	°		
I	98·4	4·000·000	4·82
II	98·0	5·100·000	5·01
III	98·6	5·200·000	5·63
IV	98·4	5·500·000	5·21
V	98·4	5·700·000	5·42

Between the highest and lowest values in this table there is a difference of 0·81 and if we look at the blood count it is seen, with one single exception,

* We desire here to acknowledge our indebtedness to our colleague, Dr. Guy Barlow, for much kindly help, and for the suggestion that led to our making and using this type of instrument.

that it rises with the number of the corpuscles present, the temperatures being almost identical. Hirsch and Beck, using much larger quantities of blood however, found with their viscosimeter that the time required by the blood of normal individuals to pass the tube varied to the extent of only 0·2 of seconds and concluded that the average viscosity might be put down as five times that of water.

As indicating the influence of the number of corpuscles upon the viscosity values we give the subjoined tables; in the one (Table IX) is shown the effect of a diminution of the number of red cells and in the other (Table X) the effect of an increase.

Table IX.—Viscosity Values in Three Cases of Marked Chlorosis.

—	Temperature.	Pulse.	Respiration.	Blood count.	Viscosity values.
	°				
I	98·0	94	24	2×10^6	2·14
II	97·6	96	26	3×10^6	3·4
III	97·8	100	26	3×10^6	3·6

Table X.—Viscosity Values in Polycythæmia.

—	Blood count.	Viscosity values.	Observer.
I	$9 \cdot 0 \times 10^6$	11·5	F. Parkes Weber*
II	$9 \cdot 0 \times 10^6$	11·8	F. Parkes Weber
III	$6 \cdot 0 \times 10^6$	6·5	F. Parkes Weber
IV	$8 \cdot 3 \times 10^6$	9·4	J. H. Watson

With regard to the influence of an increase in the number of white cells we may quote the following observations made in the wards upon a patient suffering from advanced spleno-medullary leucocythæmia, having a blood count of 2·4 million red and 76,000 white corpuscles with a temperature of 98° F.; we obtained a viscosity value of 5·6 times that of water. Here we have an apparently normal viscosity value, but if we consider the decided falling off in the number of reds, and knowing that from that cause alone there ought to be a great lowering, we are justified in assuming that the maintenance of this high value is dependent in part at least upon the presence of the excessive number of the larger leucocytes.

The above instances have been quoted as simple illustrations of the influence that changes either in the blood, whether physical or chemical, or

* F. Parkes Weber, 'Brit. Med. Jour.,' January, 1906, p. 82.

in the containing vessels may have upon the circulatory mechanism; numerous other examples might have been added; but for the present they will sufficiently serve to indicate how the work of the heart may be relieved or embarrassed by such variations. Moreover, we can thus see that the viscosity of the blood is not an independent but a dependent variable, which is essential for the maintenance of the series of adaptive changes that may occur in the circulatory system of the individual, be they physiological or pathological. And in concluding the communication we feel that the urgent need for further research in this field cannot be too strongly emphasised, in so far as even now we are still upon the borderland.

Appendix I.

Description of Clinical Viscosimeter.

The viscosimeter which we have devised for clinical purposes consists simply of a curved piece of capillary tubing with two arms. The long arm, 6 cm. in length, has been blown out at its free end into a cup-shaped receiver with a thin edge. On the short arm, about 2 cm. in length, there is a small elliptical bulb and the point at which the capillary enters and leaves the bulb is etched on the glass (*vide* fig. 10, m' and m'').

To use the Instrument.—The most convenient place to take the blood for comparative estimations of the viscosity is, in our opinion, the lobe of the ear, for not only is it less sensitive than any other part, but it can be made to bleed readily without any manipulation, whilst the position of the hanging drop permits the viscosimeter to be placed vertically. The lobe of the ear is first well cleaned with ether and a special fine pointed knife is then inserted into the most dependent part of the lobe. The viscosimeter, which has previously been warmed to the temperature of the body, is now placed underneath the hanging drop of blood and the receptacle filled. The moving thread of blood is carefully watched through its course down the long limb and bend of the tube, a stop-watch is held in readiness during this time and the seconds finger started as soon as the column of blood reaches the point m', and stopped the moment the column gains m''. The time is now read off to a fraction of a second and the result compared with the reading for water. This time value is a reliable comparative indication of the viscosity of the blood under examination. For it follows from Poiseuille's law that if the length and diameter of the viscosimeter, the quantity of fluid, and the pressure height be kept constant, and the time be observed, then the viscosity of two liquids of densities s' and s'' with times of flow t' and t'' will be as

$$n' : n'' = s't' : s''t'',$$

and hence, if we neglect the differences of densities,

$$n'/n'' = t'/t'',$$

a result which should in general be correct to about 1 per cent.

In using these tubes the following points must be observed, otherwise serious discrepancies and much difficulty will be encountered.

1. The tubes ought to be scrupulously clean and after use are best cleaned as follows:—The blood is at once driven out by a small force pump in order that clotting may not occur in the tube. The viscosimeter is then filled with strong nitric acid and placed aside for a short time, the acid is next replaced in quick succession by distilled water, alcohol and ether, and the tube finally dried by blowing a current of air through it.

2. The viscosimeter should be previously brought to the temperature of the patient.

3. It is absolutely necessary to fill the receptacle with blood, for if the column of blood in the capillary breaks from the fact that there is an insufficiency, the experiment is utterly useless on account of the altered pressure height which the method presupposes constant.

4. It is a wise precaution to fix on to the short limb of the tube a small piece of rubber tubing, so that, if the blood should at first refuse to flow through the instrument, movement may be initiated by slight suction.

5. Determinations of the viscosity of the blood should be accompanied by a careful blood count and observation of the temperature.

6. In these estimations a good assistant will be invaluable, whose care it should be to time the rate of flow.

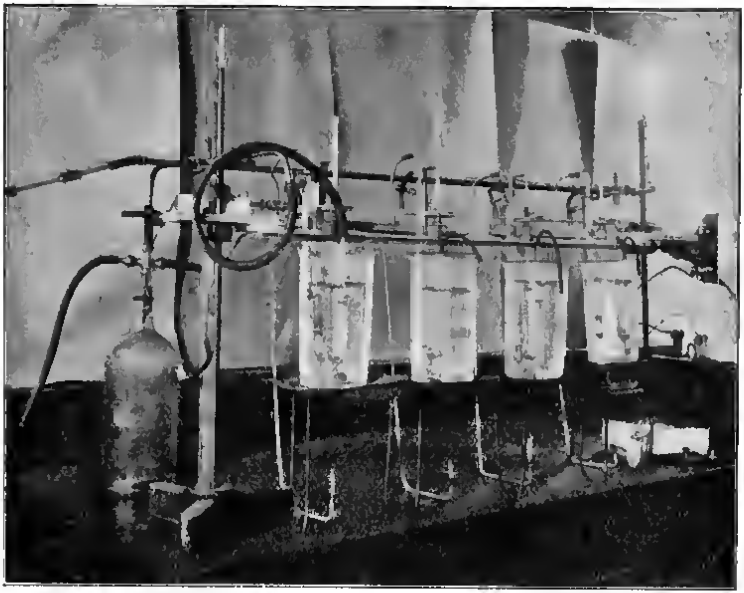

FIG. 1 A.

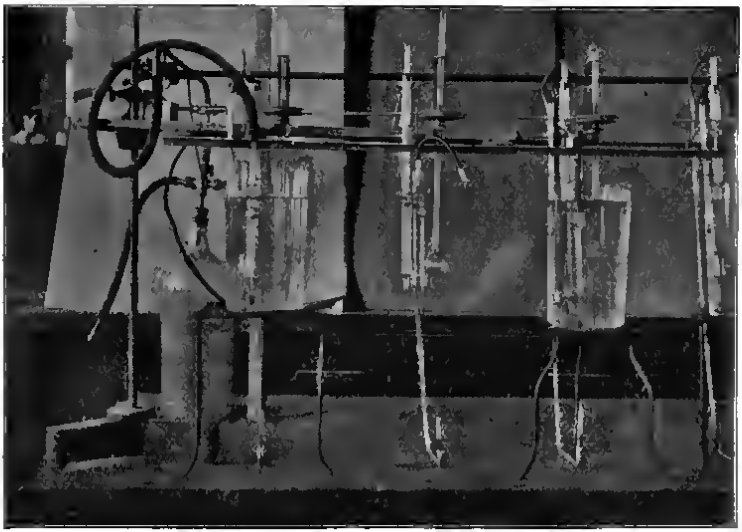

FIG. 1 B.